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Synthesis of *cis*,*cis*,*cis*-1-alkylidene-2,3,4,5-tetrakis(diphenylphosphinomethyl)cyclopentanes

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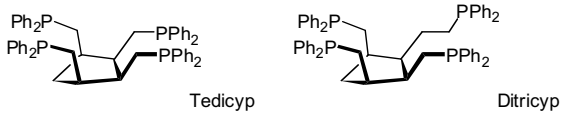
ABSTRACT

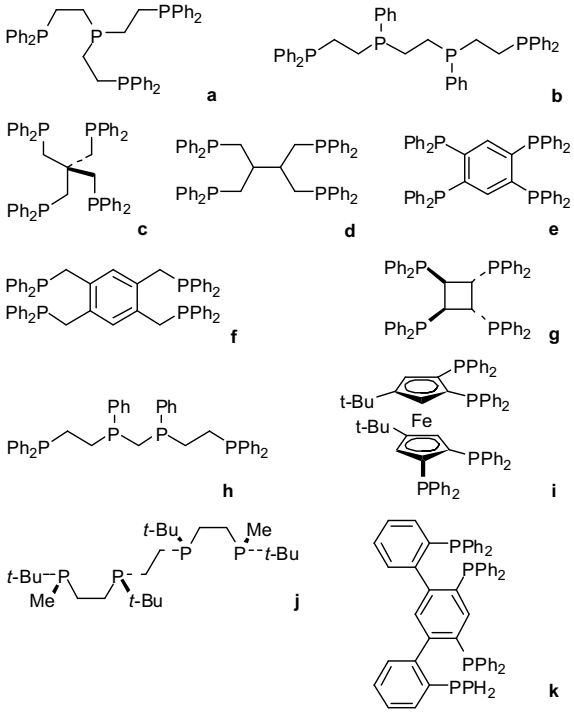
A new strategy to prepare tetradentate or pentadentate diphenylphosphine ligands has been explored from Diels–Alder adducts of fulvenes and maleic anhydride. A tetradentate phosphine ligand, bearing a side chain allowing the formation of a bond with polystyrene resin, has been prepared in seven steps from cyclopentadiene. The *cis*,*cis*,*cis*-1-cyclohexylidene-2,3,4,5-tetrakis(diphenylphosphinomethyl)-cyclopentane (Cyclo-Tedicyp) in combination with $[PdCl(C_3H_5)]_2$ led to an efficient catalyst for the Heck, Suzuki and Sonogashira coupling reactions.

1. Introduction

Chelating polyphosphine ligands are useful tools for stabilising unusual geometries in transition metal complexes. Since the last decade, our group has been investigating the synthesis and also the use in palladium-catalysed Tsuji-Trost, Heck, Suzuki, Sonogashira or Negishi coupling reactions and also the direct arylation via C–H bond activation of new tetradentate phosphine ligands, such as the *cis*,*cis*,*cis*-1,2,3,4-tetrakis(diphenylphosphinomethyl)cyclopentane (Tedicyp),[1,2] and the *cis*,*cis*,*cis*-3-(2-diphenylphosphinoethyl)-1,2,4-tris(diphenylphosphinomethyl)-cyclopentane (Ditricyp),[3] (Scheme 1). Tedicyp, and in selected cases Ditricyp, in combination with $[(\eta^3\text{-}C_3H_5)PdCl]_2$ affords catalyst precursors, which are amongst the most active for the aforementioned coupling reactions.[4]



Scheme 1.



Scheme 2.

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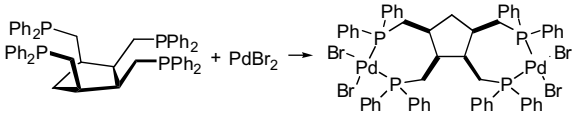
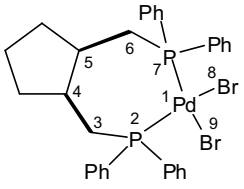
So far, only a few polypodal diphenylphosphine ligands have been synthesised[5] and generally they were only employed for hydrogenation or hydroformylation reactions.[6] It should be noted that among the tetradentate diphenylphosphino derivatives ligands, which have been prepared,[7,8] only a few of them present the specific geometry, which allows the formation of tetracoordinated complexes using only one transition metal atom (Tedicyp, **a**[7a,b], **b**[7a,b], **d**[7d], **h**[7h,i,l], **j**[7k]) (Scheme 2). In recent years, there has been an increasing interest of such polydentate ligands for the preparation of dinuclear organometallic complexes, due to their large potential in optical and/or electronic materials chemistry. On the other hand, these tetradentate ligands have been generally poorly exploited in palladium catalysis.



Scheme 3.



Bond length (Å)	Bond angle (°)
1–2: 2.283	7–1–2: 100.27
1–7: 2.276	7–1–8: 85.58
1–8: 2.473	8–1–9: 87.67
1–9: 2.465	2–1–9: 87.46
2–3: 1.838	1–2–3: 119.37
3–4: 1.531	2–3–4: 112.40
4–5: 1.538	3–4–5: 112.04
5–6: 1.523	4–5–6: 116.32
6–7: 1.826	5–6–7: 115.98
	6–7–1: 121.60
	Ph–7–Ph: 108.60
	Ph–2–Ph: 108.20

Torsional angle (°)

1–2–3–4: 42.64; 2–3–4–5: −107.92
3–4–5–6: 44.11; 4–5–6–7: 59.16
5–6–7–1: −70.61; 6–7–1–2: 3.78

Figure 1.

We believe that the efficiency of the ligand Tedicyp in palladium catalysis is due to its specific geometry, where the four diphenylphosphinomethyl groups are stereospecifically bound to the same face of the cyclopentane ring. The structure of $[(\eta^3\text{-}C_3H_5)PdCl]_2$/Tedicyp complex has been investigated by ^1H, ^{13}C and ^{31}P NMR spectra.[4] All attempts to obtain crystals from $[(\eta^3\text{-}C_3H_5)PdCl]_2$ and Tedicyp failed. However, it would be interesting to determine the geometry of the Pd/Tedicyp species. Fortunately, Tedicyp reacted with palladium(II) bromide gave a crystallised binuclear complex, suitable for X-ray analysis, which reveals that the ligand is coordinated to two palladium atoms in a symmetrical bidentate fashion (Scheme 3 and Fig. 1). The *cis*-$PdBr_2P_2$ unit is almost perfectly planar (the sums of the angles about Pd(1) and Pd(2) being 360.98 and 360.24°). As expected, the largest angle in each unit is between the two phosphorus atoms, whereas the smallest angle is between the two bromines of the seven-membered chelate ring (Fig. 2). The structure of ligands **9b** and **24** (vide infra) is very similar to the structure of Tedicyp ligand.

Actually, one of the major drawbacks of the organometallic homogeneous catalysis is the need for separation of the relative expensive, and in some cases toxic, catalysts from the reaction mixture at the end of the processes. In recent years, there has been an increasing interest in developing greener catalysed processes. In this context, supported homogeneous complexes so that catalysts can be recovered from the reaction mixture by simple filtration and reused should be convenient.[9,10] The catalyst recovery allows to decreases the contamination of the desired products with hazardous or unhealthy compounds, and also environmental pollution caused by residual toxic metals can be reduced. Consequently, the development of new polymer supported catalysts is desired.

Here, we report a new strategy, which allows the preparation of new polydentate phosphine ligands, bearing resemblance with Tedicyp, which could either be easily supported with polymers, or directly employed in palladium-catalysed reaction. In order to obtain such Tedicyp derivatives substituted on the free site of the cyclopentane ring, we have investigated a synthetic strategy involving fulvene intermediates.

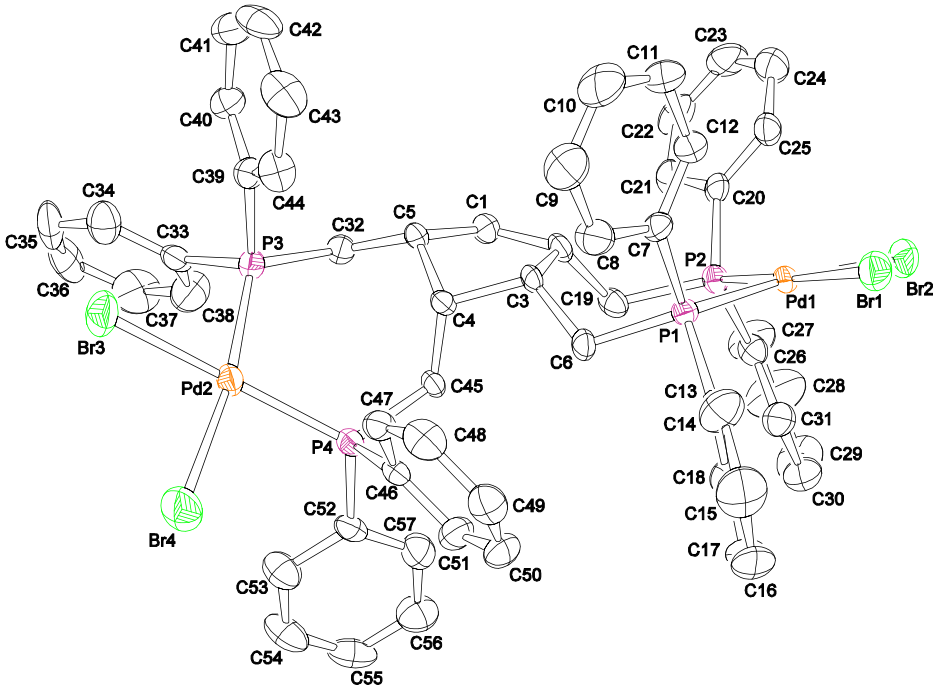
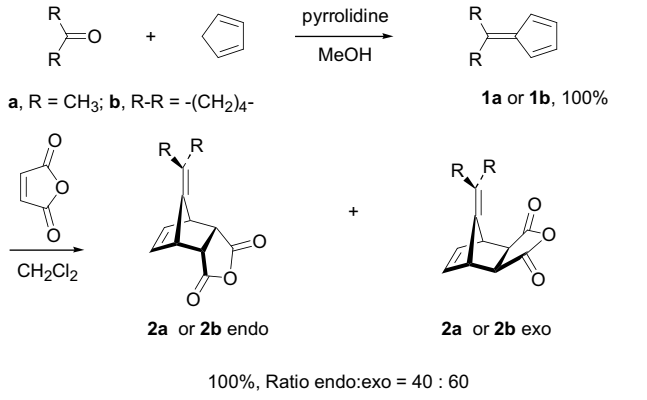


Figure 2. ORTEP diagram of Tedicyp–palladium(II) bromide complex.

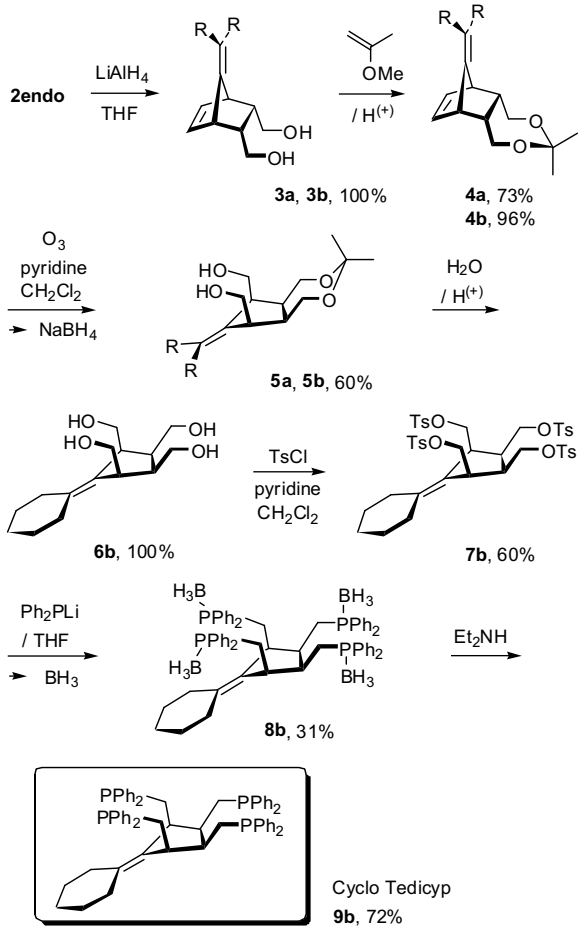
2. Results

First, the condensation of acetone or cyclohexanone with cyclopentadiene affords fulvenes **1a** or **1b** in quantitative yields.[11] Then, the Diels–Alder reaction with maleic anhydride quantitatively gave rise to a mixture of *endo* and *exo*-isomers **2a** or **2b**, which were easily separated by crystallisation (Scheme 4).[12,13]



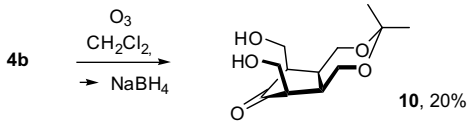
Scheme 4.

After reduction of the anhydride moiety of **2a** or **2b**, and protection of the diols **3a**,**b**, the resulting acetonides **4a**,**b** have been ozonolyzed at −60 °C in the presence of pyridine [14] and an ozonizable red dye (sudan III, Eastman Kodak) as internal standard.[15] In these conditions, only the double bond of the norbornene moiety reacts with ozone to give, after treatment with an ethanolic solution of $NaBH_4$, **5a** or **5b** in 60% yield.[3] The next steps have been conducted as usual,[1] but only with the cyclohexylidene derivatives **5b**, to give the tetraphosphine ligand Cyclo-Tedicyp **9b** in 13.4% overall yield (Scheme 5).



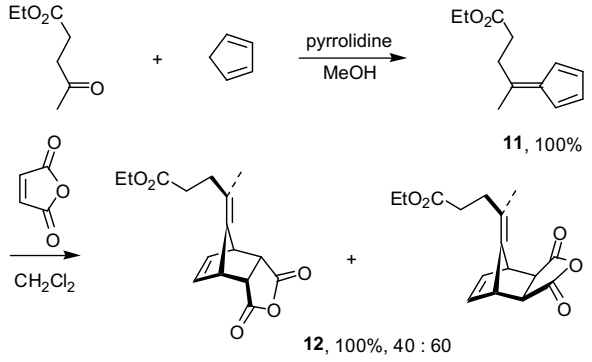
Scheme 5.

It should be noted that, when the ozonolysis of **4b** was carried out at −60 °C in absence of pyridine, the tetrasubstituted cyclopentanone **10** has been obtained in 20% yield, after the addition of $NaBH_4$ (Scheme 6).



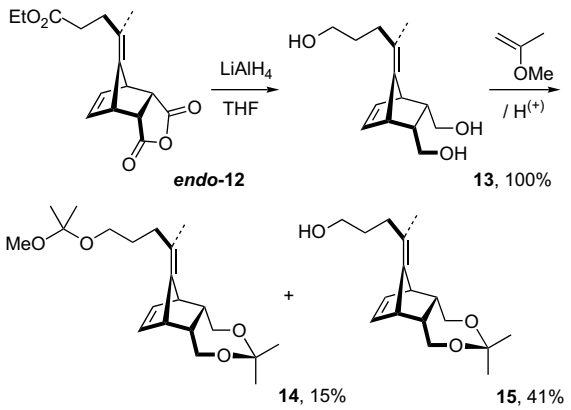
Scheme 6.

This new strategy should allow the synthesis Tedicyp derivatives bearing a tether, able to be bound to a polystyrene resin. By employing ethyl levulinate as precursor of fulvene, we have prepared the fulvene derivative **11** in quantitative yield and then, the corresponding Diels–Alder adduct **12** (Scheme 7).



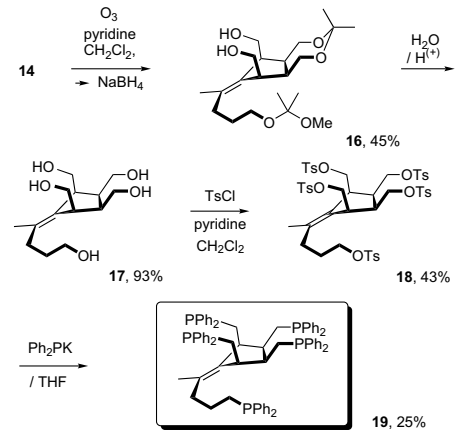
Scheme 7.

After reduction of the *endo* isomer **12** into the triol **13** and partial hydroxyl protection using an excess of 2-methoxypropene, the acetonide **15** was obtained in 41% yield. The formation of **14** in 15% yield was also observed (with an excess of 2-methoxypropene, **14** was prepared in 85% yield) (Scheme 8).

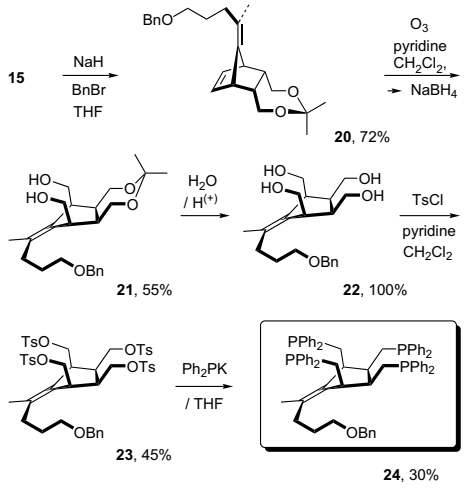


Scheme 8.

From acetonides **14** and **15**, two strategies for the access either to the desired supported ligands or to a pentadentate ligand have been investigated. From **15**, we can prepare the pentaphosphine ligand **19** (Scheme 9), while **14** gave rise to a tetraphosphine with



Scheme 9.



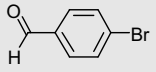
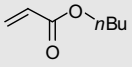
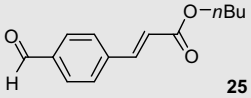
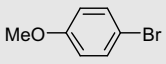
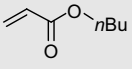
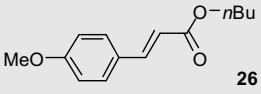
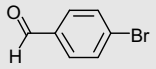
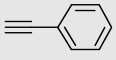
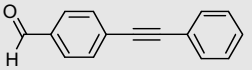
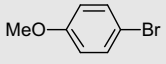
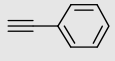
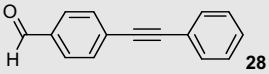
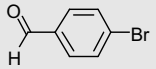
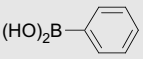
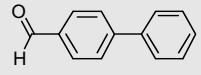
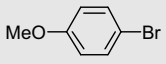
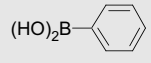
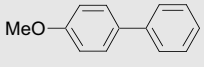
Scheme 10.

an auxiliary chain available to establish a bond with polystyrene resin (Scheme 10). The new pentatertiary phosphine ligand **19** is a chiral molecule (geometrical enantiomorphisme),[16] which should allow the formation of several cyclic chelates with transition metals.

After protection of the hydroxyl group of the side chain of **15** using benzyl bromide to form **20**, the norbornene double bond has been ozonolyzed in the presence of pyridine (Scheme 10). Again, only the double bond of the norbornene moiety reacts with ozone to give **21**. After deprotection of **21**, the tetrahydroxyl moiety was transformed into diphenylphosphino groups using an excess of Ph_2PK. Previous reports should allow the access to the supported ligand by reaction with the side chain. In the literature, several ligands, such as Binap, have been bound on commercially available polymers.[17] Our proposal was to incorporate the Tedicyp framework onto an insoluble polymer and thus provide a heterogeneous catalyst that could be isolated from the reaction medium and reused if necessary. The deprotection of benzyl group in ligand **24** can be done by reductive cleavage with calcium in liquid ammonia,[18] or with 6 N hydrochloric acid.[19] A very similar reaction has been reported by Kagan and co-workers.[20]

Here, we wish also to report the first results obtained for the catalysed Suzuki cross-coupling, Heck vinylation or Sonogashira alkynylation using Cyclo-Tedicyp **9b** as the ligand. First, we studied the Heck type coupling of an activated aryl bromide, 4-bromobenzaldehyde, with an acrylate (Scheme 1, Table 1). When 0.001 mol % of $[PdCl(C_3H_5)]_2$/Cyclo-Tedicyp was used, 100% conversion of the aryl bromide was observed (Table 1, entry 1). In the presence of 0.0001 mol % catalyst a TON (turnover number) of 460,000 was obtained (Table 1, entry 2). Next we studied the reactivity of a deactivated aryl bromide, 4-bromoanisole. As expected, a lower TON of 500 was observed, due to a slower oxidative addition of this reactant to palladium (Table 1, entry 4). Then, we examined the efficiency of ligand **9b** for the copper-free 'Sonogashira reaction' of aryl bromides with phenylacetylene. With 4-bromobenzaldehyde a TON of 1000 was obtained (Table 1, entry 6), whereas, 4-bromoanisole gave the coupling product **28** in 300 TON (Table 1, entry 8).

Table 1
Palladium/Cyclo-Tedicyp **9b** catalysed reactions

Entry	Aryl bromide	Alkene, alkyne or arylboronic acid	Ligand	Ratio substrate/catalyst	Product	Yield[a](%)
1			**9b**	100,000	 **25**	100 (92)
2			**9b**	1,000,000		100
3			**Tedicyp**	1,000,000		46[b,4a]
4			**9b**	1000	 **26**	50 (45)
5			**Tedicyp**	10,000		97[4a]
6			**9b**	1000	 **27**	100 (90)
7			**9b**	250	 **28**	100 (88)
8				1000		30
9			**9b**	1000	 **29**	100 (92)[c]
10				10,000		61[c]
11			**9b**	100,000	 **30**	100 (87)[c]
12			**Tedicyp**	100,000		(93)[c,d,4b]

Conditions: Pd–Cyclo-Tedicyp catalyst, ArBr (1 equiv), alkene, alkyne or arylboronic acid (2 equiv), K_2CO_3 (2 equiv), DMF, 130 °C, 20 h.
[a] GC and NMR conversion; yields in parenthesis are isolated.
[b] Reaction time 40 h.
[c] Reaction performed in xylene.
[d] Reaction time 24 h.

Quite surprising results were obtained for Suzuki cross-coupling. The reaction of phenylboronic acid with 4-bromobenzaldehyde gave **29** in only 6100 TON (Table 1, entry 10), whereas, in the presence of 4-bromoanisole, **30** was obtained in 100,000 TON. In summary, the reaction rates obtained with electron-deficient aryl bromides are not extremely high with this catalytic system. On the other hand, good results were obtained in the presence of the more challenging aryl bromide, 4-bromoanisole.

3. Conclusion

A straightforward and versatile synthetic route leading to various tetra- or pentaphosphine ligands has been developed from cheap reagents. The purification steps are simpler than for the previously reported synthesis of Tedicyp.[1] One of the new ligands prepared using this new strategy should allow the easy access to supported catalysts useful in organometallic chemistry. An other new tetraphosphine ligand prepared by this strategy, in combination with $[PdCl(C_3H_5)]_2$ afforded, as expected, a successful catalyst for some of the most important palladium-catalysed reactions.

4. Experimental part

4.1. General

THF was freshly distilled from sodium-benzophenone; CH_2Cl_2, triethylamine and pyridine from CaH_2 under N_2. Other reagents and solvents were obtained from commercial sources and used as received. Flash column chromatography (FC): *Merck 230–400 Mesh* silica gel; EtOAc, Et_2O and petroleum ether as eluents. Thin-layer chromatography (TLC): *Macherey–Nagel* silica gel UV_{254} analytical plates; detection either with UV, or by dipping in a solution of $KMnO_4$ (3 g), K_2CO_3 (20 g), KOH (0.3 g) in H_2O (300 mL) and subsequent heating. IR spectroscopy: *Perkin–Elmer Paragon 1600 Fourrier Transform*. NMR spectroscopy: *Bruker AC 300* (^{1}H=300 MHz, ^{13}C=75 MHz); chemical shift δ in parts per million relative to $CDCl_3$ (signals for residual $CHCl_3$ in the $CDCl_3$: 7.26 for ppm for ^{1}H NMR and 77.00 (central) for ^{13}C NMR); for the use of CD_3OD as solvent, δ=3.34 ppm for ^{1}H NMR and 49.0 ppm for ^{13}C NMR. Carbon-proton couplings were determined by DEPT sequence experiments. MS: *Applied Biosystems SCIEX QStar Elite*. Mp: not corrected. *Büchi* capillary apparatus.

4.2. 5-Cyclohexylidene-1,3-cyclopentadiene (1b)

To a stirred solution of cyclopentadiene (66 g, 1 mol) and cyclohexanone (42 mL, 0.40 mol) in methanol (1 L) under argon atmosphere was added dropwise pyrrolidine (51 mL, 0.60 mol) at room temperature. After 1 h, acetic acid (37.6 mL, 0.64 mol) was added and stirred for 0.15 h. The mixture was poured on cold water and diethyl ether was added. Aqueous layer was extracted twice with diethyl ether and the organic layer was washed with cold water, dried over $MgSO_4$, filtered and concentrated in vacuo to give **1** as a yellow oil (58.4 g, 0.40 mol), which was used for the following step without further purification. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.59 (m, 2H), 6.53 (m, 2H), 2.67 (t, J=5.4 Hz, 4H), 1.72–1.55 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 158.1 (s), 138.9 (s), 130.6 (d) (2C), 119.9 (d) (2C), 33.7 (t) (2C), 28.6 (t) (2C), 26.4 (t).

4.3. (1*S**,2*R**,6*S**,7*R**)- and (1*S**,2*S**,6*R**,7*R**)-10-Cyclohexylidene-4-oxatricyclo[5.2.1.02.6]-dec-8-ene-3,5-dione (2b)

To a stirred solution of **1b** (14.6 g, 100 mmol) in CH_2Cl_2 (300 mL) under argon atmosphere was added maleic anhydride (11.8 g, 120 mmol). After one night of stirring at room temperature, the solution was filtered and concentrated in vacuo to give a mixture of *exo* and *endo* isomers, which was recrystallised in petroleum ether–diethyl ether to give ***endo*-2b** (first crystallised) as white crystals (9.8 g, 40 mmol, 40%). Compound ***endo*-2b**, mp 132 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.44 (m, 2H), 3.96 (m, 2H), 3.52 (m, 2H), 2.03 (m, 4H), 1.46 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.7 (s) (2C), 143.1 (s), 135.8 (d) (2C), 120.8 (s), 46.7 (d) (2C), 44.7 (d) (2C), 30.4 (t) (2C), 27.7 (t) (2C), 26.3 (t).

4.4. (1*S**,2*R**,3*S**,4*R**)-7-Cyclohexylidene-2,3-di(hydroxymethyl)bicyclo[2.2.1]hept-5-ene (3b)

To a stirred suspension of $LiAlH_4$ (3.8 g, 100 mmol) in anhydrous THF (400 mL) at −20 °C under argon atmosphere was added anhydride ***endo*-2b** (12.2 g, 50 mmol) in anhydrous THF (15 mL). After one night of stirring at room temperature, the mixture was refluxing for 3 h and then cooled at −20 °C. Water (3.8 mL) followed by 3.8 mL of 1 M solution of NaOH and 11.4 mL of water was successively added. After 3 h of stirring, the suspension was filtered and washed with diethyl ether. Filtrate was concentrated in vacuo to give a white powder (11.0 g, 47 mmol, 94%) of **3b**. Mp 121 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.16 (m, 2H), 3.68 (m, 4H), 3.42 (m, 2H), 3.28 (m, 2H), 1.92 (m, 2H), 1.84 (m, 2H), 1.41 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 144.8 (s), 134.8 (d) (2C), 116.3 (s), 63.0 (t) (2C), 45.9 (d) (2C), 45.4 (d) (2C), 30.2 (t) (2C), 28.0 (t) (2C), 26.6 (t).

4.5. (1*S**,2*R**,3*S**,4*R**)-7-Cyclohexylidene-2,3-di(hydroxymethyl)bicyclo[2.2.1]hept-5-ene acetonide (4b)

To a stirred solution of **3b** (23.4 g, 100 mmol) in CH_2Cl_2 (300 mL) under argon atmosphere was added 2-methoxypropene (57 mL, 0.6 mol) and some crystals of camphorosulfonic acid. After 6 h of stirring, small amounts of anhydrous K_2CO_3 were added. After 0.5 h of stirring, the solution was filtered, concentrated in vacuo and flash chromatographed on silica gel (PE/AcOEt 95:5) to give **4b** as a yellow powder (26.3 g, 96 mmol, 96%). Mp 128 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.22 (m, 2H), 3.68 (m, 2H), 3.42 (m, 2H), 3.18 (m, 2H), 2.54 (m, 2H), 2.03 (m, 2H), 1.87 (m, 2H), 1.49 (m, 4H), 1.35 (m, 2H), 1.30 (s, 3H), 1.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 146.0 (s), 134.9 (d) (2C), 116.2 (s), 101.1 (s), 64.8 (t) (2C), 45.2 (d) (2C), 30.9 (d) (2C), 30.3 (t) (2C), 28.1 (t) (2C), 26.8 (t), 19.9 (q) (2C).

4.6. (*cis*,*cis*,*cis*)-1-Cyclohexylidene-2,3,4,5-tetra-(hydroxymethyl)cyclopentane acetonide (5b)

Ozone in oxygen was bubbled through a stirred solution of **4b** (4.1 g, 15 mmol) in CH_2Cl_2 (120 mL) and pyridine (1.2 mL) containing two drops of a CH_2Cl_2 solution of sudan III (Eastman Kodak) at −60 °C until the red colour disappeared. The mixture was flushed with argon and cooled to −80 °C. A suspension of $NaBH_4$ (1.70 g, 45 mmol) in EtOH was slowly added. After stirring at room temperature overnight, brine and EtOAc were added. Aqueous layer was extracted twice with EtOAc and the organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was recrystallised in CH_2Cl_2–Et_2O to give **5b** as a white powder (2.60 g, 8.4 mmol, 56%). Mp 118 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.05 (m, 4H), 3.61 (m, 4H), 2.10 (m, 4H), 1.42 (m, 10H), 1.36 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 136.2 (s), 131.2 (s), 102.1 (s), 63.3 (t) (2C), 62.4 (t) (2C), 44.3 (d) (4C), 31.5 (t) (2C), 28.4 (t) (2C), 26.6 (t), 24.7 (q), 24.6 (q). $C_{18}H_{30}O_4$ (310.21) C 69.64, H 9.74; found, C 69.59, H 9.71.

4.7. (*cis*,*cis*,*cis*)-1-Cyclohexylidene-2,3,4,5-tetra(hydroxymethyl)cyclopentane (6b)

To a solution of **5b** (1.55 g, 5 mmol) in THF (150 mL) and water (15 mL) was added ion exchange resin Amberlite IR® 120 hydrogen

form (2.15 g). After refluxing and stirring for 1 h, the solution was cooled to room temperature and filtrated. The solution was concentrated in vacuo. Residual water was removed by rotary distillations in vacuo using toluene. This operation was repeated twice. The crude product **6b** appeared as a yellow oil (1.35 g, 5 mmol, 100%), which was used for the following step without further purification. ^{1}H NMR (CD_3OD, 300 MHz) δ 4.77–4.01 (m, 8H), 2.87 (m, 2H), 2.74 (m, 2H), 2.22–1.50 (m, 10H); ^{13}C NMR (CD_3OD, 75 MHz) δ 134.7 (s), 133.9 (s), 63.4 (t) (2C), 60.8 (t) (2C), 47.0 (d) (2C), 45.9 (d) (2C), 31.7 (t) (2C), 28.6 (t) (2C), 26.8 (t).

4.8. (*cis*,*cis*,*cis*)-1-Cyclohexylidene-2,3,4,5-tetra-(*p*-tosyloxymethyl)cyclopentane (7b)

To a solution of *p*-tosyl chloride (63 g, 330 mmol) in CH_2Cl_2 (250 mL) and 30 mL of pyridine at −40 °C was added a solution of tetraol **6b** (2.7 g, 10 mmol) in pyridine (60 mL). The solution was stored at −20 °C for 72 h. The mixture was poured on cold water containing pyridine (60 mL) and CH_2Cl_2 (30 mL) and after stirring for 0.5 h, the organic phase was washed with a cold solution of 1 M HCl and with an aqueous solution of $CuSO_4$, dried over $MgSO_4$, filtered, concentrated in vacuo and purified by flash chromatography on silica gel (CH_2Cl_2/AcOEt 97.5:2.5) to give **7b** as a white powder (5 g, 5.6 mmol, 56%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.10 (m, 8H), 7.34 (m, 8H), 4.07 (m, 4H), 3.78 (m, 4H), 3.09 (m, 2H), 2.60 (m, 2H), 2.45 (s, 6H), 2.44 (s, 6H), 1.80 (m, 5H), 1.41 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 145.1 (s), 145.0 (s), 139.9 (s), 132.3 (s), 132.0 (s), 130.0 (d), 129.9 (d), 129.8 (d), 127.9 (d), 127.8 (d), 126.7 (s), 69.1 (t) (2C), 67.7 (t) (2C), 41.9 (d) (2C), 41.0 (d) (2C), 31.4 (t) (2C), 27.6 (t) (2C), 26.2 (t), 21.6 (q) (2C), 21.5 (q) (2C).

4.9. (*cis*,*cis*,*cis*)-1-Cyclohexylidene-2,3,4,5-tetra[(boronatodiphenylphosphanyl)methyl]-cyclopentane (8b)

To a solution of tetratosylate **7b** (886 mg, 1 mmol) in anhydrous THF (30 mL) at 0 °C under argon atmosphere was added a solution of $LiPPh_2$ in THF (~0.8 M, 19 mL, 16 mmol). After 5 h of stirring at room temperature, a 1 M solution of borane in THF (24 mL, 24 mmol) was added. After 1 h of stirring, the solution was poured on cold water and extracted with CH_2Cl_2, dried over $MgSO_4$, filtered, concentrated in vacuo and purified by flash chromatography on silica gel (PE/AcOEt 80:20) to give **8b** as a white powder (0.31 mmol, 310 mg, 31%). Mp 125 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.71–7.26 (m, 40H), 3.41 (m, 4H), 2.61 (m, 4H), 2.23 (m, 2H), 2.04 (s, 4H), 1.85 (m, 2H), 1.40 (m, 6H), 1.04 (m, 12H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.9–128.5 (50C), 38.7 (d) (2C), 37.7 (d) (2C), 31.4 (t) (2C), 30.3 (t) (2C), 21.2 (t) (2C), 26.6 (t) (2C), 26.1 (t); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 14.5 (major), 15.6, 16.6.

4.10. (*cis*,*cis*,*cis*)-1-Cyclohexylidene-2,3,4,5-tetra[(diphenylphosphanyl)methyl]cyclopentane (9b)

Compound **8b** (50 mg, 0.05 mmol) was added to anhydrous diethylamine (15 mL) and the solution was stirred at 60 °C for 2 h. The amine was removed in vacuo and the crude product was purified by flash chromatography on silica gel (PE/AcOEt 80:20) to give **9b** (34 mg, 0.036 mmol, 72%).

4.11. 5-*iso*-Propylidene-1,3-cyclopentadiene (1a)

Following the procedure previously described for the synthesis of **1b**, from acetone (30 mL, 0.4 mol), **1a** was obtained as a yellow oil, which was used for the following step without further purification. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.53–6.45 (m, 4H), 2.19 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.7 (s), 142.7 (s), 130.4 (d) (2C), 120.4 (d) (2C), 19.2 (q) (2C).

4.12. (1*S**,2*R**,6*S**,7*R**)- and (1*S**,2*S**,6*R**,7*R**)-10-*iso*-Propylidene-4-oxatricyclo[5.2.1.02.6]dec-8-ene-3,5-dione (2a)

Following the procedure previously described for the synthesis of **2b**, from **1a** (10.6 g, 100 mmol), crude **2a** in ethyl acetate gave crystals of *exo* isomer. Filtrate was purified by flash chromatography on silica gel (PE/AcOEt 80:20) to give *endo* and then *exo*-isomers. Compound ***endo*-2a**, mp 112 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.41 (m, 2H), 3.90 (m, 2H), 3.51 (m, 2H), 1.56 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.8 (s) (2C), 145.9 (s), 135.8 (d) (2C), 112.6 (s), 46.5 (d) (2C), 45.2 (d) (2C), 19.6 (q) (2C). Compound ***exo*-2a**, mp 126 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.43 (m, 2H), 3.85 (m, 2H), 3.03 (m, 2H), 1.57 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.1 (s) (2C), 139.6 (s), 137.8 (d) (2C), 116.9 (s), 49.0 (d) (2C), 46.6 (d) (2C), 19.5 (q) (2C).

4.13. (1*S**,2*R**,3*S**,4*R**)-7-*iso*-Propylidene-2,3-di(hydroxymethyl)bicyclo[2.2.1]hept-5-ene (3a)

Following the procedure previously described for the synthesis of **3b**, from **2a** (10.2 g, 50 mmol), **3a** was obtained as a white powder (9.7 g), which was used for the following step without further purification. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.19 (m, 2H), 3.64 (m, 2H), 3.42 (m, 2H), 3.27 (m, 2H), 2.49 (m, 2H), 1.59 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 147.7 (s), 134.9 (d) (2C), 134.8 (s), 63.1 (t) (2C), 46.4 (d) (2C), 45.2 (d) (2C), 19.3 (q) (2C).

4.14. (1*S**,2*R**,3*S**,4*R**)-7-*iso*-Propylidene-2,3-di(hydroxymethyl)bicyclo[2.2.1]hept-5-ene acetonide (4a)

Following the procedure previously described for the synthesis of **4b**, from **3a** (19.4 g, 100 mmol), crude product was purified by flash chromatography on silica gel (PE/AcOEt 95:5) to give **4a** as a white powder (17.1 g, 73 mmol, 73%). Compound **4a**, mp 100 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.30 (m, 2H), 3.71 (dd, J=12.9, 4.2 Hz, 2H), 3.45 (m, 2H), 3.18 (m, 2H), 2.56 (m, 2H), 1.52 (s, 6H), 1.33 (s, 3H), 1.32 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.9 (s), 134.9 (d) (2C), 107.5 (s), 101.9 (s), 64.7 (t) (2C), 45.7 (d) (2C), 44.9 (d) (2C), 29.6 (q), 19.8 (q), 19.2 (q) (2C).

4.15. (*cis*,*cis*,*cis*)-1-*iso*-Propylidene-2,3,4,5-tetra-(hydroxymethyl)cyclopentane acetonide (5a)

Following the procedure previously described for the synthesis of **5b**, from **4a** (3.51 g, 15 mmol), crude product was purified by flash chromatography on silica gel (PE/AcOEt 80:20) to give **5a** (2.43 g, 9 mmol, 60%). Compound **5a**, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.96 (m, 4H), 3.85 (m, 4H), 2.83 (m, 2H), 2.14 (m, 2H), 1.53 (s, 3H), 1.22 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 134.6 (s), 126.7 (s), 101.6 (s), 62.1 (t) (2C), 61.6 (t) (br signal), 47.2 (d) (br signal) (2C), 44.0 (d) (2C), 24.3 (q), 24.2 (q), 20.7 (q) (2C). $C_{15}H_{26}O_4$ (270.18) C 66.64, H 9.69; found, C 66.55, H 9.75.

4.16. (*cis*,*cis*,*cis*)-2,3,4,5-Tetra(hydroxymethyl)cyclopentanone acetonide (10)

Following the procedure previously described for the synthesis of **5b** but without pyridine, crude product was purified by flash chromatography on silica gel (PE/AcOEt 95:5) to give **10** in 20% yield as a yellow oil. Compound **10**, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.68 (m, 10H), 3.44 (m, 2H), 2.36 (m, 2H), 1.26 (dd, J=10.2, 6.3 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 207.2 (s), 102.0 (s), 61.1 (t) (2C), 61.0 (t) (2), 49.7 (d) (2C), 43.0 (d) (2C), 24.9 (q), 24.2 (q).

4.17. Ethyl 4-(2,4-cyclopentadien-1-ylidene)valerate (11)

To a stirred solution of cyclopentadiene (115.8 g, 1.75 mol) and ethyl levulinate (100 mL, 0.7 mol) in methanol (600 mL) under argon atmosphere was added dropwise pyrrolidine (147 mL, 1.75 mol) at room temperature. After 1 h, acetic acid (65 mL, 1.14 mol) was added and stirred for 0.15 h. The mixture was poured on cold water and diethyl ether was added. Aqueous layer was extracted twice with diethyl ether and the organic layer was washed with cold water, dried over $MgSO_4$, filtered and concentrated in vacuo to give **11** as a yellow oil (134.4 g, 0.70 mol), which was used for the following step without further purification. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.48 (m, 4H), 4.12 (q, J=7.1 Hz, 2H), 2.85 (t, J=7.6 Hz, 2H), 2.53 (t, J=7.6 Hz, 2H), 2.19 (s, 3H), 1.24 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.4 (s), 150.2 (s), 143.2 (s), 131.3 (d), 131.1 (d), 120.6 (d), 120.2 (d), 60.5 (t), 33.6 (t), 31.8 (t), 20.4 (q), 14.1 (q).

4.18. (1*S**,2*R**,6*S**,7*R**)- and (1*S**,2*S**,6*R**,7*R**)-10-(4-Ethoxycarbonylbut-2-ylidene)-4-oxatricyclo[5.2.1.0^{2,6}]-non-8-ene-3,5-dione (12)

To a stirred solution of **11** (10 g, 52.1 mmol) in CH_2Cl_2 (250 mL) under argon atmosphere was added maleic anhydride (6.13 g, 62.55 mmol). After one night of stirring at room temperature, the solution was filtered and concentrated in vacuo to give a mixture of *exo* and *endo* isomers, which was purified by flash chromatography on silica gel (petroleum ether (PE)/EtOAc 80:20) to give ***endo*-12** (4.467 g, 16.07 mmol, 31%) and ***exo*-12** (5.377 g, 19.34 mmol, 38%) as a yellow oils. Compound ***endo*-12**, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.39 (m, 2H), 4.04 (q, J=7.1 Hz, 2H), 3.97 (m, 1H), 3.85 (m, 1H), 3.54 (m, 1H), 3.45 (m, 1H), 2.30 (m, 4H), 1.55 (s, 3H), 1.22 (t, J=7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.6 (s), 170.7 (s), 170.6 (s), 147.9 (s), 135.8 (d), 135.5 (d), 115.3 (s), 60.4 (t), 46.4 (d), 46.2 (d), 45.2 (d), 45.1 (d), 32.1 (t), 28.9 (t), 16.7 (q), 14.1 (q). Compound ***exo*-12**, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.42 (m, 2H), 4.07 (q, J=7.1 Hz, 2H), 3.89 (m, 1H), 3.81 (m, 1H), 3.61 (m, 1H), 3.03 (m, 1H), 2.27 (m, 4H), 1.56 (s, 3H), 1.21 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.6 (s), 171.1 (s), 170.9 (s), 141.3 (s), 137.8 (d), 137.6 (d), 118.7 (s), 60.4 (t), 49.1 (d), 48.7 (d), 46.6 (d), 46.5 (d), 32.5 (t), 28.9 (t), 16.8 (q), 14.1 (q).

4.19. (1*S**,2*R**,3*S**,4*R**)-7-(5-Hydroxypent-2-ylidene)-2,3-di(hydroxymethyl)bicyclo[2.2.1]hept-5-ene (13)

To a stirred suspension of $LiAlH_4$ (1.22 g, 32.2 mmol) in anhydrous THF (100 mL) at −20 °C under argon atmosphere was added ***endo*-12** (4.47 g, 16.1 mmol) in anhydrous THF (15 mL). After one night of stirring at room temperature, the mixture was refluxing for 3 h and then cooled at −20 °C. Water (1.2 mL) followed by 1.2 mL of 1 M solution of NaOH and 3.6 mL of water were successively added. After 3 h of stirring, the suspension was filtered and washed with diethyl ether. Filtrate was concentrated in vacuo to give **13** as a colourless oil (3.59 g, 15.1 mmol, 94%), which was used for the following step without further purification. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.17 (m, 2H), 3.50 (m, 4H), 3.39 (m, 2H), 3.26 (m, 4H), 2.05 (m, 2H), 1.93 (m, 2H), 1.52 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.0 (s), 134.83 (d), 134.76 (d), 110.8 (s), 62.6 (t), 62.5 (t), 61.9 (t), 46.3 (d), 46.0 (d), 45.1 (d), 44.9 (d), 30.5 (t), 29.6 (t), 16.7 (q).

4.20. (1*S**,2*R**,3*S**,4*R**)-7-(5-Hydroxypent-2-ylidene)-2,3-di(hydroxymethyl)bicyclo[2.2.1]hept-5-ene acetonide (14 and 15)

To a stirred solution of **13** (15.06 g, 63.3 mmol) in CH_2Cl_2 (200 mL) under argon atmosphere was added 2-methoxypropene (12.2 mL, 126.6 mmol) and some crystals of camphorosulfonic acid. After 6 h of stirring, small amounts of anhydrous K_2CO_3 were added. After 1 h of stirring, the solution was filtered, concentrated in vacuo, and purified by flash chromatography on silica gel (CH_2Cl_2/PE 90:10) to give **14** as a yellow oil (3.28 g, 9. 37 mmol, 15%) and an **15** as an oil (7.26 g, 26.1 mmol, 41%). Compound **14**, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.23 (m, 2H), 3.67 (m, 2H), 3.43 (m, 2H), 3.27 (t, J=6.9 Hz, 2H), 3.15 (s, 3H), 3.08 (m, 2H), 2.55 (m, 2H), 1.92 (m, 2H), 1.57 (m, 2H), 1.51 (s, 3H), 1.32 (s, 3H), 1.31 (s, 3H), 1.30 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.9 (s), 134.9 (d), 134.8 (d), 110.9 (s), 101.1 (s), 99.7 (s), 64.6 (2C) (t), 60.2 (t), 48.3 (q), 45.8 (d), 45.5 (d), 45.1 (d), 44.8 (d), 30.1 (t), 29.5 (q), 28.6 (t), 24.4 (2C) (q), 19.8 (q), 16.8 (q). Compound **15**, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.24 (m, 2H), 3.69 (m, 2H), 3.51 (t, J=6.5 Hz, 2H), 3.43 (m, 2H), 3.18 (m, 2H), 2.56 (m, 2H), 1.97 (dt, J=7.5, 3.6 Hz, 2H), 1.57 (t, J=7 Hz, 2H), 1.51 (s, 3H), 1.32 (s, 3H), 1.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 150.1 (s), 134.9 (d), 134.8 (d), 110.8 (s), 101.1 (s), 64.59 (t), 64.58 (t), 62.3 (t), 45.7 (d), 45.5 (d), 45.0 (d), 44.7 (d), 30.6 (t), 29.7 (t), 29.6 (q), 19.7 (q), 16.7 (q). $C_{17}H_{26}O_3$ (278.39) C 73.34, H 9.41; found, C 73.41, H 9.68.

4.21. (*cis*,*cis*,*cis*)-1-(5-Hydroxypent-2-ylidene)-2,3,4,5-tetra(hydroxymethyl)cyclopentane derivative (16)

Ozone in oxygen was bubbled through a stirred solution of **14** (3.3 g, 9.36 mmol) in CH_2Cl_2 (100 mL) and pyridine (1.2 mL) containing two drops of a CH_2Cl_2 solution of sudan III (Eastman Kodak) at −60 °C until the red colour disappeared. The mixture was flushed with argon and cooled to −80 °C. A suspension of $NaBH_4$ (1.06 g, 28 mmol) in EtOH was slowly added. After stirring at room temperature overnight, brine and EtOAc were added. Aqueous layer was extracted twice with EtOAc and the organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (PE/EtOAc 60:40) to give **16** as a yellow oil (1.62 g, 4.2 mmol, 45%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.97 (m, 4H), 3.53 (m, 4H), 3.28 (m, 2H), 3.09 (s, 3H), 2.92 (m, 2H), 2.19 (m, 2H), 2.02 (t, J=7.8 Hz, 2H), 1.60 (s, 3H), 1.50 (m, 2H), 1.29 (s, 6H), 1.24 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.4 (s), 130.8 (s), 101.8 (s), 99.7 (s), 62.9 (t), 62.1 (t), 61.9 (t) (br signal), 61.6 (t) (br signal), 60.1 (t), 48.2 (q), 47.4 (d) (br signal), 47.2 (d) (br signal), 44.3 (d), 44.0 (d), 31.4 (t), 28.6 (t), 24.5 (q), 24.4 (q), 24.2 (q) (2C), 18.0 (q).

4.22. (*cis*,*cis*,*cis*)-1-(5-Hydroxypent-2-ylidene)-2,3,4,5-tetra(hydroxymethyl)cyclopentane (17)

To a solution of **16** (638 mg, 1.65 mmol) in THF (28 mL) and water (3 mL) was added ion exchange resin Amberlite IR® 120 hydrogen form (2.15 g). After refluxing and stirring for 1 h, the solution was cooled to room temperature and filtrated. The solution was concentrated in vacuo. Residual water was removed by rotary distillations in vacuo using toluene. This operation was repeated twice. The crude product **17** was obtained as a yellow oil (422 mg, 1.53 mmol, 93%), which was used for the following step without further purification. ^{1}H NMR (CD_3OD, 300 MHz) δ 3.79 (m, 4H), 3.53 (m, 6H), 3.02 (m, 2H), 2.49 (m, 2H), 2.11 (m, 2H), 1.69 (s, 3H), 1.60 (m, 2H); ^{13}C NMR (CD_3OD, 75 MHz) δ 137.9 (s), 131.8 (s), 64.0 (t), 63.3 (t), 62.8 (t), 61.6 (t), 61.4 (t), 48.4 (d), 47.9 (d), 46.8 (d), 46.1 (d), 32.4 (t), 32.2 (t), 18.6 (q).

4.23. (*cis*,*cis*,*cis*)-1-[5-(*p*-Tosyloxy)pent-2-ylidene]-2,3,4,5-tetra(*p*-tosyloxymethyl)cyclopentane (18)

To a solution of *p*-tosyl chloride (4.94 g, 26 mmol) in CH_2Cl_2 (10 mL) at −40 °C was added a solution of pentaol **17** (178 mg, 0.65 mmol) in pyridine (5 mL) and CH_2Cl_2 (5 mL). The solution was stored at −20 °C for 72 h. The mixture was poured on cold water

containing pyridine (2 mL) and CH_2Cl_2 (10 mL) and after stirring for 0.5 h, the solution was acidified (pH ~ 1) by addition of cold solution of HCl followed by extraction with CH_2Cl_2. The organic phase was washed with an aqueous solution of $CuSO_4$, dried over $MgSO_4$, filtered, concentrated in vacuo and purified by flash chromatography on silica gel (CH_2Cl_2/AcOEt 97.5:2.5) to give **18** as a white foam (292 mg, 0.28 mmol, 43%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.71 (m, 10H), 7.34 (m, 10H), 3.90 (m, 10H), 3.03 (m, 2H), 2.51 (m, 2H), 2.42 (s, 15H), 2.35 (t, J=6.5 Hz, 2H), 1.82 (m, 2H), 1.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 145.1 (s), 145.0 (s), 144.8 (s), 134.0 (s), 132.7 (s), 132.3 (s), 132.1 (s), 131.9 (s), 131.7 (s), 130.0 (d), 129.9 (d), 129.8 (d), 127.71 (d), 127.65 (d), 127.6 (d), 69.7 (t), 68.9 (t), 68.3 (t), 67.5 (t), 67.4 (t), 42.8 (d), 42.3 (d), 41.0 (d), 40.6 (d), 30.7 (t), 26.8 (t), 21.5 (q), 21.46 (q), 21.40 (q), 18.0 (q).

4.24. (*cis*,*cis*,*cis*)-1-[5-(Diphenylphosphanyl)pent-2-ylidene]-2,3,4,5-tetra(diphenylphosphanylmethyl)cyclopentane (19)

To a solution of pentatosylate **18** (200 mg, 0.202 mmol) in anhydrous THF (10 mL) at 0 °C under argon atmosphere was added a solution of $KPPh_2$ in THF (8.1 mL, 4.04 mmol) (Fluka). After 5 h of stirring at room temperature, 2 mL of MeOH was added and the solution was concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (PE then PE/Et_2O 90:10) (these eluents were previously degassed under argon atmosphere) to give **19** as a wax (56 mg, 0.05 mmol, 25%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.34 (m, 50H), 2.40 (m, 10H), 1.57 (m, 4H), 1.44 (s, 3H), 0.96 (m, 2H), 0.86 (m, 2H); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ −15 (3P), −18 (2P).

4.25. (1*S**,2*R**,3*S**,4*R**)-7-(5-Benzyloxypent-2-ylidene)-2,3-di(hydroxymethyl)bicyclo[2.2.1]hept-5-ene acetonide (20)

To a suspension of NaH (0.28 g, 7.05 mmol) in anhydrous THF (30 mL) at 0 °C under argon atmosphere was added a solution of alcohol **15** (1.31 g, 4.70 mmol) and tetrabutylammonium iodide (0.13 g, 0.47 mmol) in anhydrous THF (10 mL). The solution was stirred for 1 h at room temperature and cooled to 0 °C. Then, benzyl bromide (1.12 mL, 9.40 mmol) was added. After stirring at room temperature for 1 h, the solution was refluxed for 7 h. The solution was poured on cold water and extracted with CH_2Cl_2. The organic phase was washed with water, dried over $MgSO_4$, filtered, concentrated in vacuo and purified by flash chromatography on silica gel (PE/AcOEt 90:10) to give **20** (1.24 g, 3.38 mmol, 72%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.32 (m, 5H), 6.25 (m, 2H), 4.49 (s, 2H), 3.70 (m, 2H), 3.46 (m, 2H), 3.40 (t, J=6.5 Hz, 2H), 3.19 (m, 2H), 2.58 (m, 2H), 1.99 (td, J=7.6, 2.3 Hz, 2H), 1.65 (t, J=7.2 Hz, 2H), 1.53 (s, 3H), 1.36 (s, 3H), 1.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 150.2 (s), 138.6 (s), 134.9 (d), 128.3 (d) (2C), 127.6 (d) (3C), 127.4 (d), 110.7 (s), 101.1 (s), 72.8 (t), 69.7 (t), 64.7 (t), 64.6 (t), 45.8 (d), 45.6 (d), 45.1 (d), 44.8 (d), 29.9 (t), 29.6 (q), 28.0 (t), 19.9 (q), 16.8 (q).

4.26. (*cis*,*cis*,*cis*)-9-(5-Benzyloxypent-2-ylidene)-8,10-di(hydroxymethyl)-4,4-dimethyl-3,5-dioxa-bicyclo[5.3.0]decane acetonide (21)

Following the procedure previously described for the ozonolysis of **14**, from 19 (1 g, 2.72 mmol), **21** was obtained as a yellow oil (540 mg, 1.48 mmol, 55%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.28 (m, 5H), 4.46 (s, 2H), 4.02 (m, 4H), 3.55 (m, 4H), 3.41 (t, J=6.2 Hz, 2H), 2.95 (m, 2H), 2.10 (m, 4H), 1.70 (m, 2H), 1.64 (s, 3H), 1.35 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.2 (s), 135.6 (s), 130.8 (s), 128.2 (d)(2C), 127.5 (d), 127.4 (d), 101.8 (s), 72.8 (t), 69.9 (t), 63.0 (t), 62.1 (t), 62.0 (t), 61.6 (t), 47.3 (d)(2C), 44.3 (d), 44.0 (d), 31.3 (t), 28.2 (t), 24.4 (q) (2C), 18.0 (q). $C_{24}H_{36}O_5$ (404.26) C 71.26, H 8.97; found, C 71.33, H 9.03.

4.27. (*cis*,*cis*,*cis*)-1-(5-Benzyloxypent-2-ylidene)-2,3,4,5-tetra(hydroxymethyl)cyclopentane (22)

Following the procedure previously described for the hydrolysis of **16**, from **21** (113 mg, 0.28 mmol), **22** was obtained as a yellow oil (102 mg, 0.28 mmol, 100%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.28 (m, 5H), 4.47 (s, 2H), 3.81 (m, 2H), 3.46 (m, 8H), 3.02 (m, 2H), 2.44 (m, 2H), 2.15 (m, 2H), 1.66 (m, 2H), 1.43 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 136.0 (s), 135.7 (s), 130.7 (s), 128.3 (d) (2C), 127.7 (d), 127.6 (d), 72.8 (t), 70.0 (t), 62.8 (t) (br signal), 62.0 (t) (br signal), 60.5 (t) (2C), 46.8 (d), 46.4 (d), 45.3 (d), 44.4 (d), 31.2 (t), 27.9 (t), 20.9 (q).

4.28. (*cis*,*cis*,*cis*)-1-[5-(Benzyloxy)pent-2-ylidene]-2,3,4,5-tetra(*p*-tosyloxymethyl)cyclopentane (23)

Following the procedure previously described for the preparation of **18**, from **22** (112 mg, 0.31 mmol), **23** was obtained as a colourless oil (133 mg, 0.136 mmol, 45%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.73 (m, 5H), 7.28 (m, 12H), 4.44 (s, 2H), 4.04 (m, 4H), 3.90 (m, 4H), 3.34 (t, J=6.1 Hz, 2H), 3.10 (m, 2H), 2.52 (m, 2H), 2.44 (s, 9H), 2.42 (s, 3H), 2.37 (m, 2H), 1.90 (m, 2H), 1.45 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 145.1 (s), 145.1 (s), 145.0 (s), 138.3 (s), 135.5 (s), 132.4 (s), 132.2 (s), 132.13 (s), 132.11 (s), 130.7 (s), 130.04 (d), 130.01 (d), 129.9 (d), 128.3 (d), 127.8 (d), 127.7 (d), 127.5 (d), 127.4 (d), 72.8 (t), 69.4 (t), 69.1 (t), 68.5 (t), 67.7 (t) (2C), 42.9 (d), 42.4 (d), 41.4 (d), 40.8 (d), 31.4 (t), 27.8 (t), 21.6 (q), 21.5 (q), 18.2 (q).

4.29. (*cis*,*cis*,*cis*)-1-(5-Benzyloxypent-2-ylidene)-2,3,4,5-tetra(diphenylphosphanylmethyl)cyclopentane (24)

Following the procedure previously described for the preparation of **19**, from **23** (200 mg, 0.20 mmol), **24** was obtained as a colourless wax (40 mg, 0.039 mmol, 19%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.33 (m, 45H), 4.28 (br d, J=2.4 Hz, 2H), 2.93 (t, J=6.9 Hz, 2H), 2.37 (m, 8H), 1.59 (m, 4H), 1.43 (s, 3H), 1.03 (s, 2H), 0.86 (m, 2H); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ −14.3 (dd, J=12.5, 8.0 Hz), −16.1 (dd, J=10.2, 7.6 Hz), −18.4 (dd, J=13.2, 3.5 Hz), −18.8 (dd, J=10.5, 3.8 Hz).

4.30. (1*S**,2*R**,3*S**,4*R**)-7-(5-*tert*-Butyldimethylsilyloxypent-2-ylidene)-2,3-di(hydroxymethyl)bicyclo[2.2.1]hept-5-ene acetonide (24a)

To a solution of **14** (548 mg, 1.97 mmol) in anhydrous DMF (20 mL) under argon atmosphere was added imidazole (0.271 g, 3.98 mmol) and *tert*-butyldimethylsilyl chloride (0.362 g, 2.39 mmol). After stirring for one night at room temperature, the solution was poured on cold water and the mixture was extracted with Et_2O (three times) and the organic phase was washed with water, dried over $MgSO_4$, filtered and concentrated in vacuo to give **24a** as a yellow oil (688 mg, 1.76 mmol, 90%), which was used for the following step without further purification. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.23 (m, 2H), 3.68 (m, 2H), 3.53 (t, J=6.5 Hz, 2H), 3.44 (m, 2H), 3.15 (m, 2H), 2.55 (m, 2H), 1.90 (m, 2H), 1.53 (m, 2H), 1.52 (s, 3H), 1.32 (s, 3H), 1.31 (s, 3H), 0.87 (s, 9H), 0.02 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.9 (s), 134.9 (d), 134.8 (d), 110.9 (s), 101.1 (s), 64.6 (2C) (t), 62.5 (t), 45.8 (d), 45.5 (d), 45.1 (d), 44.8 (d), 31.3 (t), 29.6 (t), 29.5 (q), 25.9 (q) (3C), 19.8 (q), 18.2 (s), 16.9 (q), −5.33 (2C)(q).

4.31. (1*S**,2*R**,3*S**,4*R**)-7-(5-Triphenylsilyloxypent-2-ylidene)-2,3-di(hydroxymethyl)bicyclo[2.2.1]hept-5-ene acetonide (24b)

Following the procedure previously described for the preparation of **24a**, from **14**, **24b** was obtained, which was used for the following step without further purification. ^{1}H NMR ($CDCl_3$,

300 MHz) δ 7.68 (m, 6H), 7.41 (m, 9H), 6.24 (m, 1H), 6.17 (m, 1H), 3.78 (t, J=6.5 Hz, 2H), 3.68 (td, J=12.1, 4.1 Hz, 2H), 3.43 (m, 2H), 3.13 (m, 2H), 2.53 (m, 2H), 2.00 (t, J=7.5 Hz, 2H), 1.63 (m, 2H), 1.51 (s, 3H), 1.39 (s, 3H), 1.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.9 (s), 135.3 (d) (6C), 134.2 (s) (3C), 134.8 (d), 134.4 (d), 129.9 (d) (3C), 127.8 (d) (6C), 110.9 (s), 101.3 (s), 64.7 (t), 64.6 (t), 63.6 (t), 45.7 (d), 45.5 (d), 45.0 (d), 44.7 (d), 31.0 (t), 29.7 (t), 29.6 (q), 19.8 (q), 16.8 (q).

4.32. (*cis*,*cis*,*cis*)-9-(5-(*tert*-Butyldimethylsilyloxy)pent-2-ylidene)-8,10-di(hydroxymethyl)-4,4-dimethyl-3,5-dioxabicyclo[5.3.0]decane (25a)

Following the procedure previously described for the ozonolysis of **4**, from **24a** (1.46 g, 3.70 mmol), **25a** was obtained as a yellow oil (1.00 g, 2.33 mmol, 63%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.01 (m, 4H), 3.54 (m, 6H), 2.93 (m, 2H), 2.02 (m, 2H), 1.62 (s, 3H), 1.51 (m, 2H), 1.33 (s, 6H), 1.25 (m, 2H), 0.84 (s, 9H), 0.01 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.2 (s), 131.2 (s), 101.9 (s), 63.0 (t), 62.8 (2C) (t), 62.7 (t), 62.2 (t), 46.3 (d), 45.1 (d), 44.4 (d), 44.1 (d), 31.4 (t), 31.1 (t), 25.8 (q) (3C), 24.6 (q), 24.5 (q), 18.2 (q), 14.6 (s), −5.4 (q) (2C).

4.33. (*cis*,*cis*,*cis*)-9-(5-(Triphenylsilyloxy)pent-2-ylidene)-8,10-di(hydroxymethyl)-4,4-dimethyl-3,5-dioxabicyclo[5.3.0]decane (25b)

Following the procedure previously described for the ozonolysis of **4**, from **24b** (2.84 g, 5.30 mmol), **25b** was obtained as a yellow foam after a flash chromatography on silica gel (1.22 g, 2.12 mmol, 40%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.62 (m, 6H), 7.41 (m, 9H), 3.99 (m, 4H), 3.80 (td, J=6.3, 1.2 Hz, 2H), 3.56 (m, 4H), 2.94 (m, 2H), 2.26 (m, 2H), 2.10 (m, 2H), 1.68 (m, 2H), 1.63 (s, 3H), 1.38 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.4 (d) (6C), 135.3 (s), 134.2 (s) (3C), 131.2 (s), 130.0 (d) (3C), 101.9 (s), 63.6 (t) (2C), 63.1 (t), 62.4 (t), 61.8 (t), 47.0 (d) (2C), 44.3 (d) (2C), 31.2 (t), 31.1 (t), 24.7 (q), 24.6 (q), 18.3 (q).

4.34. Crystal data and structure refinement for Tedicyp–2 $PdBr_2$ crystals

The complex co-crystallised together with three full occupancy acetonitrile molecules and a fourth disordered one with a partial occupancy of 0.25.

Crystallographic data: $C_{63.5}H_{63.75}Br_4N_{3.25}P_4Pd_2$, M_w=1528.75, monoclinic, yellow crystal (0.15×0.1×0.05 mm^3), a=17.4630(3) Å, b=22.4740(4) Å, c=18.0690(3) Å, β=117.3151(1)°, V=6300.70(19) Å^3, space group $P2_1/c$, Z=4, ρ=1.612 g cm^{-3}, μ(Mo Kα)=3.25 cm^{-1}, 14,723 unique reflections in the 1.31–29.0° θ range, 697 parameters refined on F^2 [Shelxl] to final indices $R[F^2>4\sigma F^2]$=0.05 (6965 reflections), $wR[w=1/[\sigma^2(F_o^2)]$=0.1034 (all reflections). The last residual Fourier positive and negative peaks were equal to 0.880 and −1.049, respectively.

4.35. Preparation of the Pd/Cyclo-Tedicyp catalyst

An over-dried 40-mL Schlenk tube equipped with a magnetic stirring bar, under argon atmosphere, was charged with $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (9.2 mg, 0.025 mmol) and Cyclo-Tedicyp (47.2 mg, 0.05 mmol). Anhydrous DMF (5 mL) was added, then the solution was stirred at room temperature for 20 min. This solution was used directly for the catalysed reactions.

4.36. General procedure for the coupling of *n*-butyl acrylate, phenylacetylene or phenylboronic acid with aryl bromides

The reaction of the aryl bromide (1 mmol), K_2CO_3 (2.76 g, 2 mmol) and *n*-butyl acrylate, phenylacetylene or phenylboronic acid (2 mmol) at 130 °C during 20 h in DMF or xylene (10 mL) (see Table 1) in the presence of the Cyclo-Tedicyp/palladium complex under argon affords the corresponding coupling products **25–30** after addition of water, extraction with dichloromethane or ether, separation, drying ($MgSO_4$), evaporation and filtration on silica gel.

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